

### **REMARKS/ARGUMENTS**

Claims 1-65 were pending in the present application before this amendment as set forth above. By this amendment, claims 1, 12, 19, 21-23, 29, 30, 33, 50-56, and 60 are amended and claims 17, 18, and 49 are canceled without prejudice. Also, the specification has been amended to identify related applications and to correct informalities.

In the December 18, 2008 Office Action, the Examiner rejected claims 1-9, 14-16, 60, 61, 64, and 65 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent Pub. 2006/0194273 to Thomas (hereinafter “Thomas”). Also, claims 1-5, 8-17, 33-38, 41-48 and 57-65 were rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent Pub. 2003/0003571 to Kanegasaki et al. (hereinafter “Kanegasaki”). Further, claims 18-24 and 49-56 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kanegasaki, as applied to claim 17, and further in view of U.S. Patent Pub. 2002/0086280 to Lynes et al. (hereinafter “Lynes”). In addition, claims 25-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki, as applied to claim 1, and further in view of U.S. Patent Pub. 2004/0142409 to Allen et al. (hereinafter “Allen”). Moreover, claims 39 and 40 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kanegasaki, as applied to claim 33, and further in view of Thomas.

In the December 18, 2008 Office Action, the Examiner also asserted that the disclosure of the prior-filed application, Application No. 60/406,278 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. §112 for one or more claims in the application and that accordingly, these claims are not awarded the priority date established by the prior-filed application.

Furthermore, claims 1-5, 8-11, 14-16, 33-38, 41-48, and 60-65 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44-49 and 58-65 of copending Application No. 10/525,559. Moreover, claims 1-65 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-77 of copending Application No. 10/525,538.

Applicant very much appreciates the Examiner’s careful review of the instant application. Applicant particularly thanks Primary Examiner Beisner and Examiner Bowers for granting and conducting a telephone interview held March 24, 2009 with Dr. Tim Xia, a Patent Attorney for Applicant on the record, Mr. Christopher Glass, a Patent Attorney, and Dr. John Wikswo, an

Inventor. Applicant also appreciates very much the professionalism shown by Primary Examiner Beisner and Examiner Bowers during the telephone interview.

During the telephone interview, the December 18, 2008 Office Action was discussed, and particularly independent claims 1, 33 and 60 of the present invention. Applicant proposed amendments to claims 1, 33, and 60 that recited to means adapted for electrochemical measurements of cells. Primary Examiner Beisner indicated that this limitation differentiated the claims from the cited references.

In response, as set forth above, claims 1, 12, 19, 21-23, 29, 30, 33, 50-56, and 60 have been amended for better form. Specifically, claim 1 has been amended to incorporate the limitations of original claim 12 and now canceled claims 17 and 18, and claims 33 and 60 have been amended to incorporate the limitations of now canceled claim 49. Each of the amended independent claims 1, 33 and 60 incorporate limitations of means for electrochemical measurements of cells as suggested in the March 24, 2009 interview.

Without acquiescing in the propriety of the Examiner's rejections and to facilitate the prosecution of the current application, as set forth above, claims 17, 18, and 49 have been canceled, which makes the Examiner's rejections under 35 U.S.C. §102(e) and 35 U.S.C. §103(a) moot. Applicant reserves every right in these canceled claims to file continuation and divisional applications.

Support for the amendments can be found in the disclosure as originally filed, for example in the claims as originally filed, in paragraphs from page 20, lines 25-38 through page 28, lines 1-6 of the specification and Figs. 1A, 1B, and 2 of the drawings. Applicant submits that no new matter has been added.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical correction only.

It is now believed that the application is in condition for allowance at least for the reasons set forth below and such allowance is respectfully requested.

The following remarks herein are considered to be responsive thereto.

***Priority***

In the December 18, 2008 Office Action, the Examiner asserted that the disclosure of the prior-filed provisional application 60/406,278 fails to provide adequate support or enablement under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner asserted that “Application 60/406,278 does not describe the use of a barrier to divide a chamber into a first subchamber and a second subchamber, wherein the barrier has a porosity to allow the permeation of a predetermined cell type” and that accordingly, “claims requiring this limitation are not awarded the priority date established by Application No. 60/406,278.”

Applicant respectfully traverses this assertion, and submits that adequate support can be found in the disclosure of the provisional application 60/406,278, as originally filed, for example, in paragraphs on lines 5-29 of page 28 and in Fig. 1 of Appendix A. Fig. 1 shows a barrier 102/104 to divide a chamber into two (or more) chambers. *Adequate support* is therefore provided for the claims at issue and Applicant respectfully requests that the priority date established by Application No. 60/406,278 be awarded accordingly.

***Claim Rejections under 35 U.S.C. § 102***

In the December 18, 2008 Office Action, the Examiner rejected claims 1-9, 14-16, 60, 61, 64, and 65 under 35 U.S.C. § 102(e) as being anticipated by Thomas. Also, claims 1-5, 8-17, 33-38, 41-48 and 57-65 are rejected under 35 U.S.C. § 102(e) as being anticipated by Kanegasaki.

Applicant respectfully traverses these rejections for at least the following reasons.

***Claims 1-16:***

As set forth above, claim 1, as amended, recites “a bioreactor for cultivating living cells in a liquid medium comprising:

- a. a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving the cells and the liquid medium;
- b. a barrier dividing the chamber into a first subchamber and a second subchamber, wherein the barrier has a porosity to allow the first subchamber and the second subchamber in fluid communication and allow at least one predetermined type of cells to permeate between the first subchamber and the second subchamber;

- c. *a second substrate positioned adjacent to the first surface of the first substrate;*
- d. *a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate; and*
- e. *means positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber.”* (Emphasis added.)

As disclosed in paragraphs on page 20, lines 24-38 through page 24, lines 1-20 of the specification and as shown in Figs. 1A and 1B of the drawings, as originally filed, in one embodiment a bioreactor 100 has “a first substrate 140 having a first surface 140a and an opposite second surface 104b, defining a chamber 101 therebetween for receiving cells and a liquid medium. The bioreactor 100 has a barrier 104 dividing the chamber 101 into a first subchamber 102 and a second subchamber 103, wherein the barrier 104 has a porosity to allow the first subchamber 102 and the second subchamber 103 in fluid communication and allow at least one predetermined type of cells to permeate between the first subchamber 102 and the second subchamber 103... Moreover, *the bioreactor 100 has a second substrate 150, wherein the second substrate 150 is positioned adjacent to the first surface 140a of the first substrate 140* and defines a plurality of connection channels 155... The bioreactor 100 further has *a third substrate 160*, which is positioned adjacent to the first surface of the first substrate 140, *and means 161-165 strategically positioned in the third substrate 160 and adapted for electrochemical measurements of the cells responsive to the liquid medium in one or both of the first subchamber 102 and the second subchamber 103.* In one embodiment as shown in Fig. 1B, the *means for electrochemical measurements* includes a reference electrode 161, a counter electrode 162, a plurality of edge connector pads 164,...a plurality of electrically conductive leads 163,...[and] a plurality of individually addressable working electrodes 165.” (Emphasis added.)

In contrast, as understood by Applicant, Thomas discloses an “apparatus for performing cell growth and cell based assays and methods for performing such assays.” (Thomas, [0002].) For example, Fig. 1B of Thomas shows a rotatable disc 18 having an annular sample reservoir 9 connected to a plurality of assay elements 6, a sample inlet channel and an outlet channel for

removal of liquid, and a cover plate positioned onto the disc. (Thomas, [0027].) Thomas simply *does not* disclose, teach, or suggest a bioreactor having “*a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate; and[,] means positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber*” and having all of the other limitations recited in amended claim 1. (Emphasis added.)

Moreover, as understood by Applicant, Kanegasaki discloses “a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor.” (Kanegasaki, [0009].) In one embodiment as shown in Fig. 3, for example, a “well unit [including a substrate 7 and a substrate 8] has a channel 1 and wells 2A and 2B in which a sample such as a cell suspension or a specimen solution is contained. A sample is supplied into the well 2A or 2B through a tube 3A or 3B with the use of a micropipette, etc. After [cell] migration, cells are collected from the well 2A or 2B through the tube 3A or 3B.” (Kanegasaki, [0088].) Kanegasaki also discloses that for detection of this cell migration, “use can be made of, for example, a microscope [see, e.g. *microscope 13 externally disposed in relation to the well unit*]” and further discloses that “[f]or detection in integrated [well] units, *it is preferable* to employ a system wherein the channels of the units are successively scanned along with *an objective lens*.” (Kanegasaki, [0162] - [0165].) In the December 18, 2008 Office Action, the Examiner conceded on page 7 that Kanegasaki *does not* disclose a third substrate including a means for electrochemical measurements. Moreover, Kanegasaki *does not* disclose, teach, or suggest a bioreactor having “*a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate; and[,] means positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber*” and having all of the other limitations recited in amended claim 1. (Emphasis added.)

Thus, neither Thomas nor Kanegasaki disclose, teach, or suggest a bioreactor having all of the limitations as recited in claim 1, as amended.

For at least these reasons, Applicant submits that independent claim 1, as amended, is not anticipated under 35 U.S.C. §102(c) and is patentable over each of Thomas and Kanegasaki.

Accordingly, claims 2-16 and 19-32, which depend from allowable amended claim 1, are also patentable at least for these reasons.

**Claims 33-48 and 50-59:**

As set forth above, claim 33, as amended, recites “a bioreactor for cultivating living cells in a liquid medium comprising:

- (a) a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving the cells and the liquid medium, wherein the chamber is formed with a center and a boundary;
- (b) a first barrier enclosing the center and a portion of the chamber to form a central chamber;
- (c) a second barrier positioned between the first barrier and the boundary so as to form an intermediate chamber and an outer chamber; and
- (d) ***means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber and the central chamber,***

wherein the first barrier has a first porosity to allow the central chamber and the intermediate chamber in fluid communication and allow at least a first predetermined type of cells to permeate between the central chamber and the intermediate chamber, and the second barrier has a second porosity to allow the outer chamber and the intermediate chamber in fluid communication and allow at least a second predetermined type of cells to permeate between the outer chamber and the intermediate chamber.” (Emphasis added.)

As disclosed in paragraphs on page 24, lines 22-38 through page 27, lines 1-34 of the specification and as shown in Fig. 2 of the drawings, as originally filed, in one embodiment, a bioreactor 700 “includes a substrate 730 having a first surface and an opposite second surface, defining a chamber 732 therebetween for receiving cells and a liquid medium, wherein the

chamber 732 is formed with a center 734 and a boundary 736. The bioreactor 700 also has a first barrier 738, which encloses the center 734 and a portion of the chamber 732 to form a central chamber 706, and a second barrier 740, which is positioned between the first barrier 738 and the boundary 736 so as to form an intermediate chamber 705 and an outer chamber 704. In [this] embodiment, the first barrier 738 has a first porosity to allow the central chamber 706 and the intermediate chamber 705 in fluid communication and allow at least a first predetermined type of cells to permeate between the central chamber 706 and the intermediate chamber 705, and the second barrier 740 has a second porosity to allow the outer chamber 704 and the intermediate chamber 705 in fluid communication and allow at least a second predetermined type of cells to permeate between the outer chamber 704 and the intermediate chamber 705...*The bioreactor 700 further includes means strategically positioned and adapted for electrochemical measurements of the cells responsive to the liquid medium in one or more of the outer chamber 704, the intermediate chamber 705 and the central chamber 706.*In [the] embodiment as shown in Fig. 2, the means for electrochemical measurements includes a reference electrode 707, a counter electrode 708, and a plurality of individually addressable working electrodes 709-711.” (Emphasis added.)

In contrast, as set forth above and as understood by Applicant, Kanegasaki discloses “a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor.” (Kanegasaki, [0009].) In one embodiment as shown in Fig. 12, for example, Kanegasaki discloses a well unit including channel(s) 1, wells 2A-2C, penetrating holes 3a, 4a, and a substrate 7. As conceded by the Examiner on page 7 of the December 18, 2008 Office Action, Kanegasaki does not disclose means for electrochemical measurements. Moreover, Kanegasaki *does not* disclose, teach, or suggest a bioreactor having “*means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber and the central chamber,*” and having all of the other limitations recited in amended claim 33. (Emphasis added.)

For at least these reasons, Applicant submits that independent claim 33, as amended, is not anticipated under 35 U.S.C. §102(e) and is patentable over Kanegasaki. Accordingly, claims

34-48 and 50-59, which depend from allowable amended claim 33, are also patentable at least for these reasons.

**Claims 60-65:**

As set forth above, claim 60, as amended, recites “a bioreactor for cultivating living cells in a liquid medium comprising:

- (a) a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving the cells and the liquid medium with a boundary; and
- (b) means for dividing the chamber into plurality of chambers; and
- (c) *means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the plurality of chambers,*

wherein each of the plurality of subchambers is in fluid communication with at least another one of the plurality of subchambers.” (Emphasis added.)

Support for the amendment can be found in the disclosure as originally filed, for example, in paragraphs on page 12, lines 37-38 through page 13, lines 1-2 of the specification and in Fig. 2 of the drawings.

Incorporating herein the reasons set forth above why amended claim 33 is not anticipated under 35 U.S.C. § 102(e), Applicant respectfully submits that independent claim 60, as amended, is patentable for at least these reasons.

Accordingly, claims 61-65, which depend from now allowable amended claim 60, are also patentable for at least this reason.

**Claim Rejections under 35 U.S.C. § 103**

In the December 18, 2008 Office Action, claims 25-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki, as applied to claim 1, and further in view of U.S. Patent Pub. 2004/0142409 to Allen et al. (hereinafter “Allen”). Moreover, claims 39 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, as applied to claim 33, and further in view of Thomas. However, these rejections are moot, in light of amendments to now allowable independent claims 1 and 33, as set forth above.



***Double Patenting***

In the December 18, 2008 Office Action, claims 1-5, 8-11, 14-16, 33-38, 41-48, and 60-65 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44-49 and 58-65 of copending Application No. 10/525,559. Moreover, claims 1-65 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-77 of copending Application No. 10/525,538.

Applicant respectfully submits the copending Application No. 10/525,559 has been issued as U.S. Patent No. 7,534,601, on May 19, 2009.

In response, without acquiescing to the propriety of the rejections and in order to facilitate the prosecution of the present application, Applicant respectfully submits herewith, as suggested by the Examiner, two Terminal Disclaimers to overcome these double patenting rejections.


### CONCLUSION

Applicant respectfully submits that the foregoing Response places this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner's amendment, to facilitate the prosecution, please call the undersigned at 404.495.3678. The Commissioner is hereby authorized to charge any petition fee under 37 CFR 1.17(f),(g) or (h) or any deficiency of fees and credit of any overpayments to Deposit Account No. 50-3537.

Respectfully submitted,

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